**Dry Eye Syndrome**

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*A/E = androgen/estrogen ratio*
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--Facilitating diffusion of oxygen to the avascular cornea;
--clearing debris from the corneal surface; and
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The tear film resides in the tear strip/lake resting on the lower-lid margin, and is pulled up and onto the ocular surface via the action of the upper lid.
Dry Eye Syndrome

Tear lake (aka tear strip; tear meniscus)
**Dry Eye Syndrome**

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Dry Eye Syndrome

The tear film is comprised of three basic components: Lipid, aqueous, and mucin. These components interact to produce the two-phase model of the tear film: The aqueous and mucus intermix into a single, gel-like layer (the mucoaqueous phase), which is covered by the lipids in a lipid phase.
Two-phase model of the tear film. Schematic drawing of the structure of the tear film showing the outer lipid layer and the mucoaqueous layer.
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The older tripartite model of the tear film posited that the three components formed distinct mucus (inner), aqueous (middle) and lipid (outer) layers, but the consensus now is this model is incorrect, and it has largely been supplanted by the two-phase model.
Dry Eye Syndrome

The old/obsolete *tripartite model* of the tear film
The tear film is comprised of three basic components: Lipid, aqueous, and mucin. These components interact to produce the two-phase model of the tear film. The older tripartite model posited three distinct layers: mucus (inner), aqueous (middle), and lipid (outer). However, the consensus now is that this model is incorrect and has largely been supplanted by the two-phase model.

Dry Eye Syndrome

The specific lipid is meibum, a product of the meibomian glands. These glands are embedded within the tarsal plates of both the upper and lower lids. There are ~2x as many glands in the upper lids. They are innervated by the parasympathetic system.
Dry Eye Syndrome

Meibomian glands
Dry Eye Syndrome

Upper lid

Lower lid

Meibomian glands
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The lipid layer makes several key contributions to the stability and effectiveness of the tear film. It inhibits tear film evaporation and reduce its surface tension, both of which serve to maintain the tear film on the eye. (Without a lipid layer, surface tension would pull the tear film down off the surface.) The lipid layer also facilitates visual acuity by producing a glassy-smooth surface at the air-tear film interface.
The tear film is comprised of three basic components: **Lipid**, **aqueous**, and **mucin**. These components interact to produce the **two-phase model** of the tear film: The aqueous and mucin intermix into a single, gel-like layer (the **mucoaqueous phase**), which is covered by the lipids in a **lipid phase**.

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**Dry Eye Syndrome**

**Aqueous** is produced by the **lacrimal glands**, which includes the **main lacrimal gland** (found in the superotemporal orbit) and the accessory lacrimal glands of **Krauss** and **Wolfring** (found scattered throughout the forniceal and palpebral conj). All of the lacrimal glands are innervated by parasympathetics as well.
Dry Eye Syndrome

The main lacrimal gland
Dry Eye Syndrome

The lacrimal glands of Krause and Wolfring
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**Mucin** is produced by goblet cells located in the conjunctival epithelium, and also are parasympathetically innervated. The chief function of the mucin component of the mucoaqueous layer is facilitating ocular-surface wetting.
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We saw this depiction of the *two-phase model of the tear film* earlier in the set. But are now ready to note the presence and location of mucin. Note that there are ‘membrane-bound’ mucins in the glycocalyx of the corneal epithelium.
Dry Eye Syndrome

The tear film contains a number of constituent molecules that serve important roles in ocular health. Among these are **proteins** and **electrolytes**.
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The tear film contains a number of constituent molecules that serve important roles in ocular health. Among these are proteins and electrolytes. The main protein to be aware of is IgA, which plays a key role in ocular-surface defense. The primary role of electrolytes in the tear film is to regulate tear-film osmolarity. Recall that osmolarity refers to the concentration of solutes in a fluid—literally, the number of solute-particles in a given amount of fluid. Normal tear osmolarity is $296 \pm 10$ milliosmoles per liter (mOsm/L).
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Dry Eye Syndrome

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But why is tear-film osmolarity important? For one reason: The osmotic-pressure gradient it can exert on the underlying ocular-surface epi cells. The membranes of these cells are freely permeable to water but not solutes (ie, they are semi-permeable). Recall the rule regarding semi-permeable membranes: Solvent follows solute.
Dry Eye Syndrome

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Next we turn to the concept of the **lacrimal functional unit** (LFU). The LFU is the system responsible for the regulation, production, and health of the tear film.
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Recall that a reflex arc has three components: A *sensory limb* consisting of sensory receptors and afferent nerves, a *motor limb* consisting of efferent nerves and the effector end-organ, and a *CNS integration center* that connects the afferent and efferent limbs.

Next we turn to the concept of the *lacrimal functional unit* (LFU). The LFU is the system responsible for the regulation, production, and health of the tear film. *Think of it as a ‘reflex arc’ responsible for the production of the components of the tear film.*
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Next we turn to the concept of the **lacrimal functional unit** (LFU). The LFU is the system responsible for the regulation, production, and health of the tear film. *Think of it as a ‘reflex arc’ responsible for the production of the components of the tear film.*
We are ready (finally!) to tackle the pathophysiology of DES…
Dry Eye Syndrome

The pathophysiology for DES damage starts with derangement of the tear film in the form of Tear Hyperosmolarity.

We are ready (finally!) to tackle the pathophysiology of DES… Which commences with tear hyperosmolarity

Tear hyperosmolarity
Dry Eye Syndrome

The pathophysiology for DES damage starts with derangement of the tear film in the form of Tear Hyperosmolarity.

There are two basic ways in which the status of the aqueous component of the tear film could lead to tear hyperosmolarity:
Dry Eye Syndrome

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1) The amount of aqueous produced can be inadequate to maintain normal osmolarity. 

or...

Tear hyperosmolarity
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There are two basic ways in which the status of the aqueous component of the tear film could lead to tear hyperosmolarity:

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Dry Eye Syndrome

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1) The amount of aqueous produced can be inadequate to maintain normal osmolarity. This state is known as... *Aqueous Tear Deficiency*

2) The amount of aqueous lost can be too high to maintain normal osmolarity.
Dry Eye Syndrome

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1) The amount of aqueous produced can be inadequate to maintain normal osmolarity. This state is known as Aqueous Tear Deficiency.

2) The amount of aqueous lost can be too high to maintain normal osmolarity. This state is known as Evaporative Dry Eye.

Tear hyperosmolarity
Dry Eye Syndrome

The pathophysiology for DES damage starts with derangement of the tear film in the form of **Tear Hyperosmolarity**.

There are two basic ways in which the status of the aqueous component of the tear film could lead to tear hyperosmolarity:

While it’s a bit of an oversimplification, we can associate the components of the tear film with the pathologic states underlying DES:
Dry Eye Syndrome

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- Problem with the aqueous component
  - Aqueous Tear Deficiency

Evaporative Dry Eye

Tear hyperosmolarity
Dry Eye Syndrome

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- **Problem with the *aqueous component***
  - *Aqueous Tear Deficiency*

- **Problem with the *lipid component***
  - *Evaporative Dry Eye*
There are two basic ways in which the status of the aqueous component of the tear film could lead to tear hyperosmolarity:

- Aqueous Tear Deficiency
- Evaporative Dry Eye

Head’s up: Shortly we’re gonna add a third mechanism leading to tear hyperosmolarity.
Evaporative Dry Eye

Dry Eye Syndrome

The pathophysiology for DES damage starts with derangement of the tear film in the form of Tear Hyperosmolarity.

Let’s drill down on both, starting with ATD.

- Problem with the **aqueous component**
  - Aqueous Tear Deficiency

- Problem with the **lipid component**
  - Evaporative Dry Eye

Tear hyperosmolarity
The pathophysiology for DES damage starts with derangement of the tear film in the form of Tear Hyperosmolarity.

**But first—**

Let’s drill down on both, starting with ATD.

- **Problem with the aqueous component**
  - Aqueous Tear Deficiency
- **Problem with the lipid component**
  - Evaporative Dry Eye

Tear hyperosmolarity
Dry Eye Syndrome

**But first—there are three classic tests of aqueous tear production:**

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Dry Eye Syndrome

Aqueous tear production testing
But first—there are three classic tests of aqueous tear production:

*What each assesses: How each is performed: How each is interpreted:*

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Dry Eye Syndrome

ATD is subdivided into two categories: Sjögren’s and non-Sjögren’s

Sjögren’s

Non-Sjögren’s

Aqueous Tear Deficiency

Evaporative Dry Eye

Tear hyperosmolarity
Sjögren’s syndrome (SS) is a chronic autoimmune disorder characterized by lymphocytic infiltration of exocrine glands. The vast majority of pts are female. It is divided into primary and secondary forms, the key distinction being that secondary SS is associated with a systemic connective-tissue disease (eg, RA, SLE, scleroderma).
Sjögren’s syndrome (SS) is a chronic autoimmune disorder characterized by lymphocytic infiltration of exocrine glands. The vast majority of pts are female. It is divided into primary and secondary forms, the key distinction being that secondary SS is associated with a systemic connective-tissue disease (eg, RA, SLE, scleroderma). In both forms, aqueous hyposcretion (and thus ATD) results from autoimmune-mediated lymphocytic infiltration of the lacrimal glands.
In non-Sjögren’s ATD, other causes of lacrimal gland hyposcretion are at work:

- Lacrimal duct obstruction
- Reflex block
- Systemic drug effect

Non-Sjögren’s

Aqueous Tear Deficiency

Tear hyperosmolarity
**Reflex block** refers to anything that disrupts the normal functioning of the LFU ‘reflex circuit.’

(A no-frills version of the LFU for reference)
**Dry Eye Syndrome**

**Reflex block** refers to anything that disrupts the normal functioning of the LFU ‘reflex circuit.’ *Afferent* limb block is often due to corneal hypoesthesia from corneal surgery, post-herpetic neuropathy, and contact-lens wear.
**Dry Eye Syndrome**

**Reflex block** refers to anything that disrupts the normal functioning of the LFU ‘reflex circuit.’ *Afferent* limb block is often due to corneal hypoesthesia from corneal surgery, post-herpetic neuropathy, and contact-lens wear. *Efferent* limb block is usually due to compromised CN7 function, eg, Bell’s palsy.

(A no-frills version of the LFU for reference)
A substantial number of systemic drugs are implicated in inducing DES. (Eg, 22 of the 100 best-selling drugs in the US list ‘dry eye’ as a side effect!)

**Dry Eye Syndrome**

- Lacrimal duct obstruction
- Reflex block

**Systemic drug effect**

**Non-Sjögren’s**

- Aqueous Tear Deficiency
- Evaporative Dry Eye

**Tear hyperosmolarity**
A substantial number of systemic drugs are implicated in inducing DES. (Eg, 22 of the 100 best-selling drugs in the US list ‘dry eye’ as a side effect!) These include anti-histamines, anti-cholinergics (eg, antidepressants), anti-hypertensives, Parkinson’s meds, and OCPs (because of their effect on androgens and estrogen).
Dry Eye Syndrome

EDE is also subdivided into two categories: Intrinsic and Extrinsic

Intrinsic

Extrinsic

Evaporative
Dry Eye

Aqueous Tear Deficiency

Tear hyperosmolarity

Sjögren's
Dry Eye Syndrome

Sjögren’s Syndrome is associated with dry eye due to decreased aqueous tear production.

EDE is also subdivided into two categories: **Intrinsic** and **Extrinsic**. In this context, *intrinsic EDE* refers to any cause related to the eyelids, whereas *extrinsic EDE* refers to any non-eyelid factor that promotes evaporation.
Dry Eye Syndrome

There are three common causes of intrinsic EDE:

- Meibomian gland dysfunction (MGD)
- Widened lid fissure
- Reduced blink rate

Sjögren’s

Non-Sjögren’s

Aqueous Tear Deficiency

Tear hyperosmolarity

Extrinsic

Evaporative Dry Eye

Intrinsic
MGD refers to a broad group of disorders characterized by dysfunction of the meibomian glands. Individuals of Asian heritage are at especially high risk.
MGD refers to a broad group of disorders characterized by dysfunction of the meibomian glands. Individuals of Asian heritage are at especially high risk. In many cases, the dysfunction is due to obstruction of gland output leading to an inadequate volume of meibum in the tear-film; in others, the meibum’s chemical composition has been altered, rendering it ineffective. (Chemical alteration and obstruction commonly co-exist in the same pt.)
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We will have more to say about MGD later in the set.
A *widened lid fissure* can be secondary to forward displacement of the globe (i.e., proptosis/exophthalmos); increased innervation to the lid retractors such as occurs in thyroid eye disease; and/or to congenital craniofacial malformations resulting in shallow orbits (e.g., Crouzon syndrome).
Dry Eye Syndrome

TED: Lid retraction + exophthalmos -> surface exposure -> EDE
Dry Eye Syndrome

Crouzon syndrome: Shallow orbits->surface exposure->EDE
Dry Eye Syndrome

Causes of **reduced blink rate** include normal phenomena such as seen during sustained participation in a visually intensive task (e.g., reading; computer work) as well as pathological causes such as Parkinson’s dz.

- **Intrinsic**
  - Meibomian gland dysfunction (MGD)
  - Widened lid fissure
- **Extrinsic**
- **Evaporative Dry Eye**
- **Aqueous Tear Deficiency**
- **Tear hyperosmolarity**

Sjögren’s  Non-Sjögren’s

Reduced blink rate
There are two basic ways in which the status of the aqueous component of the tear film could lead to tear hyperosmolarity:

- Aqueous Tear Deficiency
- Evaporative Dry Eye

Head’s up: Shortly we’re gonna add a third mechanism leading to tear hyperosmolarity.

Recall that earlier in the set we alluded to a third means by which tear-film status could produce hyperosmolarity and dry eye. The time to address this has arrived!
The pathophysiology for DES damage starts with derangement of the tear film in the form of Tear Hyperosmolarity.

The other fundamental way could the status of the tear film lead to tear hyperosmolarity:

- Aqueous Tear Deficiency
- Evaporative Dry Eye

Tear hyperosmolarity
Dry Eye Syndrome

The pathophysiology for DES damage starts with derangement of the tear film in the form of 
**Tear Hyperosmolarity.**

*The other fundamental way could the status of the tear film lead to tear hyperosmolarity:*

The tear film can break up too quickly, exposing the ocular surface.

Aqueous Tear Deficiency  
?  
↓  
Tear hyperosmolarity  
Evaporative Dry Eye
Dry Eye Syndrome

The pathophysiology for DES damage starts with derangement of the tear film in the form of Tear Hyperosmolarity.

The other fundamental way could the status of the tear film lead to tear hyperosmolarity:

The tear film can break up too quickly, exposing the ocular surface.
This state is known as one of...
Dry Eye Syndrome

The pathophysiology for DES damage starts with derangement of the tear film in the form of Tear Hyperosmolarity.

Recalling our answers to this issue previously:

While it’s a bit of an oversimplification, we can associate the components of the tear film with the pathologic states underlying DES:

- **Problem with the aqueous component**
  - Aqueous Tear Deficiency

- **Problem with the lipid component**
  - Evaporative Dry Eye

Tear Film Instability

Tear hyperosmolarity
Evaporative Dry Eye

The pathophysiology for DES damage starts with derangement of the tear film in the form of **Tear Hyperosmolarity**.

Recalling our answers to this issue previously:

With respect to tear-film instability, problems with the mucin (and lipid) components lead to tear-film instability.
Teardrop instability is quantified via the tear-film break-up time (TBUT or TFBUT) assessment. A little fluorescein is instilled, and the pt is asked to hold their eyes open after blinking a couple of times.
Tear-film instability is quantified via the **tear-film break-up time** (TBUT or TFBUT) assessment. A little fluorescein is instilled, and the pt is asked to hold their eyes open after blinking a couple of times. The tear film is observed with the cobalt-blue filter in place, and the length of time that passes until a dry spot appears is noted. A TBUT of less than ~10s is considered abnormal.
Three categories of conditions leading to TFI have been identified:

- **Sjögren’s**
- **Non-Sjögren’s**
- **Aqueous Tear Deficiency**

**Tear Film Instability**

- **Xerophthalmia**
- **Topical preservatives**
- **Ocular allergy**

**Evaporative Dry Eye**

**Tear hyperosmolarity**
The leading cause of xerophthalmia worldwide is **hypovitaminosis A**, a potentially fatal condition.
The leading cause of xerophthalmia worldwide is **hypovitaminosis A**, a potentially fatal condition. Hypovitaminosis A xerosis of the ocular surface produces **Bitôt spots**—foamy, white/gray area on the interpalpebral conjunctiva.
Bitôt spots: Conj finding temporal to the cornea, with typical dry/foamy appearance
Preservatives in ophthalmic preparations lead to TFI by provoking an inflammatory response in the conj epithelium, which in turn promotes goblet cell apoptosis.
Preservatives in ophthalmic preparations lead to TFI by provoking an inflammatory response in the conj epithelium, which in turn promotes goblet cell apoptosis. The preservative benzalkonium chloride (aka BAK or BAC) is especially notorious for doing this.
Allergic antigens produce TFI by initiating an IgE-mediated inflammatory cascade, leading to goblet-cell loss.
Dry Eye Syndrome

Now that we understand how ATD, TFI and EDE lead to tear hyperosmolarity...
Now that we understand how ATD, TFI and EDE lead to tear hyperosmolarity…
Let’s examine how tear hyperosmolarity leads to DES
Evaporative Dry Eye

Dry Eye Syndrome

Surface epithelium damage

Hyperosmolar stress

First:
Tear-film hyperosmolarity initiates the DES cascade by stressing surface epithelium, significantly damaging it.

Aqueous Tear Deficiency

Tear Film Instability

E evaporative Dry Eye

Tear hyperosmolarity
Dry Eye Syndrome

Then:
In turn, damaged epi cells release cytokines that promote and/or facilitate inflammation. These cytokines include TNF, MMP-9, and IL-1.

Inflammatory cytokine release

Surface epithelium damage

Hyperosmolar stress

Tear-film hyperosmolarity initiates the DES cascade by stressing surface epithelium, significantly damaging it.

Aqueous Tear Deficiency

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Evaporative Dry Eye

Tear hyperosmosmolarity
Then:
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Tear-film hyperosmolarity initiates the DES cascade by stressing surface epithelium, significantly damaging it.

Note that surface epi damage induces cytokine release... And cytokine release induces surface epi damage. Thus, a vicious cycle/circle develops in which epi damage leads directly to further epi damage.

Evaporative Dry Eye

Aqueous Tear Deficiency

Tear Film Instability

Tear hyperosmosmolarity
**Dry Eye Syndrome**

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**Note that**

Cytokines also impede function of the afferent arm of the LFU reflex arc…

Tear-film hyperosmolarity initiates the DES cascade by stressing surface epithelium, significantly damaging it.
Evaporative Dry Eye Syndrome

**Note that**
Cytokines also impede function of the afferent arm of the LFU reflex arc...resulting in decreased aqueous production.

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Tear-film hyperosmolarity initiates the DES cascade by stressing surface epithelium, significantly damaging it. So neural reflex arc disruption decreases aqueous production…

And decreased aqueous production worsens tear hyperosmolarity, which in turn starts the entire process over again. Thus, a vicious cycle/circle develops in which decreased aqueous production leads directly to further decreases in aqueous production.
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Dry Eye Syndrome

Increased aqueous production

Neural reflex arc disruption

Increased aqueous production

Aqueous Tear Deficiency

Tear Film Instability

Evaporative Dry Eye

Tear hyperosmolarity
In turn, damaged epi cells release cytokines that promote and/or facilitate inflammation. These cytokines include TNF, MMP-9, and IL-1. TNF and IL-1 promote epi-cell apoptosis, whereas MMP-9 cleaves epi cells from their BM.

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Tear-film hyperosmolarity initiates the DES cascade by stressing surface epithelium, significantly damaging it.

So neural reflex arc disruption decreases aqueous production…And decreased aqueous production worsens tear hyperosmolarity, which in turn starts the entire process over again. Thus, another vicious cycle/circle develops in which decreased aqueous production leads directly to further decreases in aqueous production.

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Dry Eye Syndrome

- Decreased aqueous production
- Neural reflex arc disruption
- Inflammatory cytokine release
- Surface epithelium damage
- Hyperosmolar stress

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

- Aqueous Tear Deficiency
- Tear Film Instability
- Evaporative Dry Eye
Dry Eye Syndrome

Decreased aqueous production

Neural reflex arc disruption

Inflammatory cytokine release

Surface epithelium damage

Hyperosmolar stress

1) Increase tear volume

Tear Film Instability

Evaporative Dry Eye

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:
Dry Eye Syndrome

Decreased aqueous production

Neural reflex arc disruption

Inflammatory cytokine release

Surface epithelium damage

Hyperosmolar stress

1) Increase tear volume

2) Decrease tear evaporation

Aqueous Tear Volume Tear Film Instability Tear evaporation Evaporative Dry Eye

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:
Dry Eye Syndrome

Decreased aqueous production

Neural reflex arc disruption

Tear Film Instability

Surface epithelium damage

Hyperosmolar stress

Tear evaporation

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

1) Increase tear volume
2) Decrease tear evaporation
3) Prevent cytokine release and/or mitigate their effects
Dry Eye Syndrome

Decreased aqueous production

Neural reflex arc disruption

1) Increase tear volume

2) Decrease tear evaporation

3) Prevent cytokine release and/or mitigate their effects

The most straightforward means of increasing aqueous volume is supplementing the tear lake with artificial tears. (The Cornea book says tear substitutes are “the mainstay of treatment for aqueous tear deficiency.”)

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:
Dry Eye Syndrome

1) Increase tear volume
2) Decrease tear evaporation

3) Prevent cytokine release and/or mitigate their effects

The most straightforward means of increasing aqueous volume is supplementing the tear lake with artificial tears. (The Cornea book says tear substitutes are “the mainstay of treatment for aqueous tear deficiency.”)

In more severe cases punctal occlusion may be indicated.

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:
With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

1) Increase tear volume
   - *Aqueous Tear Volume*

2) Decrease tear evaporation
   - *Tear Film Instability*

3) Prevent cytokine release and/or mitigate their effects
   - *Inflammatory Cytokine Release*

The mainstay tx of EDE is **lid hygiene**. (The *Cornea* book says lid hygiene is “an essential part [of tx] at all stages of the disease.”)
With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

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2) Decrease tear evaporation
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The mainstay tx of EDE is **lid hygiene**. (The *Cornea* book says lid hygiene is “an essential part [of tx] at all stages of the disease.”)

The two fundamental steps involved in lid hygiene are:
1) Application of heat to the eyelids to soften the abnormal meibum; and
2) Compression/massage of the lid margin to express the abnormal meibum.
Dry Eye Syndrome

Decreased aqueous production

1) Increase tear volume
2) Decrease tear evaporation
3) Prevent cytokine release and/or mitigate their effects

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

Quick sidebar on ‘abnormal meibum’: What makes it abnormal is its chemical composition, which has been altered (and not for the better). Because of this altered composition, its melting point is higher than normal. Normal meibum is a liquid at body temperature, which is why expressed normal meibum looks like tiny drops of vegetable oil resting on the lid margin. In contrast, the chemically-altered meibum in MGD is a semisolid at body temp, which is why expressed abnormal meibum looks like toothpaste. So not only is the meibum in MGD altered (and thus less effective), the fact that it’s a semisolid means it can’t even get out of the glands and onto the tear film.
Dry Eye Syndrome

Normal meibum
With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

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2) Decrease tear evaporation
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Dry Eye Syndrome

Ewwww
Dry Eye Syndrome

Decreased aqueous production

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With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

1) Increase tear volume
2) Decrease tear evaporation

Tear Film Instability

Tear evaporation

Evaporative Dry Eye
Dry Eye Syndrome

Decreased aqueous production

Tear Film Instability

Surface epithelium damage

Hyperosmolar stress

Inflammatory cytokine release

Decreased aqueous production

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

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So to reiterate, the logic underpinning lid hygiene is:

--Step 1: Liquify the semisolid abnormal meibum clogging the glands
--Step 2: Express the now-liquefied abnormal meibum from the glands
Dry Eye Syndrome

Decreased aqueous production

But using heat and massage to get the abnormal meibum flowing is not sufficient. Why? Because once the lids cool back down to body temp, the subsequent (abnormal) meibum will again be semisolid—that is, unless steps are taken to normalize its chemical composition.

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

1) Increase tear volume

2) Decrease tear evaporation

Hyperosmolar stress

Tear volume

Aqueous Tear

Tear Film

Instability

Evaporative Dry Eye

Tear evaporation

Topical abx to reduce bacterial load (bacterial lipases play an important role in altering meibum's chemical composition)

Topical steroids and nonsteroidal anti-inflammatories

PO tetracyclines—not as an antibacterial, but for its anti-inflammatory properties (it reduces cytokine release and inhibits MMP-9 activity)
Dry Eye Syndrome

Decreased aqueous production

1) Increase tear volume

1) Increase tear volume

2) Decrease tear evaporation

2) Decrease tear evaporation

With regards to treating DES—there are three obvious interdiction points in its pathogenesis:

- **Tear volume**: Reduced tear production leads to decreased tear film volume.
- **Tear evaporation**: Increased tear evaporation results in a thinner tear film.
- **Tear Film Instability**: Instability of the tear film due to factors like surface epithelium damage or neural reflex arc disruption.

Hyperosmolar stress

- **Decreased aqueous production**
- **Tear Film Instability**
- **Tear evaporation**

But using heat and massage to get the abnormal meibum flowing is not sufficient. Why? Because once the lids cool back down to body temp, the subsequent (abnormal) meibum will again be semisolid—that is, unless steps are taken to normalize its chemical composition. To accomplish this, interventions include:

- Topical abx to reduce bacterial load (bacterial lipases play an important role in altering meibum’s chemical composition)
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Dry Eye Syndrome

Decreased aqueous production

Hypermolar stress

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3) Prevent cytokine release and/or mitigate their effects

Tear Film Instability

Tear evaporation

Aqueous Tear Volume

Evaporative Dry Eye

Tear

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- Topical steroids and **nonsteroidal anti-inflammatories**
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Two steroid-sparing topical anti-inflammatories are used in the US: Cyclosporine and lifitegrast. Both work by interfering with the activation and/or function of T-cells.
Dry Eye Syndrome

Decreased aqueous production

To this point we’ve discussed treatment strategies for ATD and EDE as distinct entities (which they are). However, ATD and EDE frequently coexist in DES pts, and this has important implications for management. Most interventions (ATs, anti-inflammatory meds) are useful in both conditions. However, there is one relatively common ATD intervention that must be used with caution in pts who also have MGD: Punctal occlusion.

Aqueous Tear Deficiency

Tear Film Instability

Evaporative Dry Eye

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Finally: The *Cornea* book discusses several conditions that mimic DES in their presentation:

--Conjunctivochalasis
--Superior limbic keratoconjunctivitis (SLK)
--Floppy eyelid syndrome
--Nighttime lagophthalmos
--Parkinson’s
--Mucous-membrane pemphigoid/OCP
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Conj’chalasis refers to loose, redundant, nonedematous conj. It usually manifests as a ‘fold’ of conj draping on the lower-lid margin.
Dry Eye Syndrome

Conjunctivochalasis
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Conj’chalasis refers to loose, redundant, nonedematous conj. It usually manifests as a ‘fold’ of conj draping on the lower-lid margin. The cause is likely mechanical trauma of the lids rubbing against the bulbar conj during blinking. The redundant conj chafes against itself during blinking and eye movements, causing conj’chalasis pts to have many of the same symptoms as DES pts: FBS, red eyes, and tearing.
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Conj’chalasis is managed in a stepwise manner. It’s reasonable to start with ATs, antihistamines, steroids etc—although one of the characteristics of conj’chalasis is that it doesn’t respond well to DES-tx maneuvers. Often, surgical intervention (in the form of excision or thermal cicatrization) is required for resolution.
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--**Superior limbic keratoconjunctivitis (SLK)**

**SLK** is a chronic/recurrent inflammatory condition of the superior limbal cornea and adjacent conj. It is rare, and the vast majority of sufferers are women. SLK pts share many of the same symptoms as DES pts (FBS, red eyes, and tearing). However, the *signs* in the two differ enough to allow them to be distinguished from one another.
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Dry Eye Syndrome

K and conj staining in SLK vs DES
Dry Eye Syndrome

SLK: Superior conj injection
Dry Eye Syndrome

Superior rose bengal staining

Superior lissamine green staining

SLK: Superior conj staining
Dry Eye Syndrome

SLK: Superior corneal filaments
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Dry Eye Syndrome

SLK: Superior tarsal conj papillary rxn
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The pathogenesis of the superior conj/cornea damage in SLK stems from excessive contact and rubbing between the upper lid and the superior conj/cornea. SLK pts have overly tight superior lids, usually as a result of orbital congestion stemming from thyroid eye dz—a classic (and highly testable) association with SLK.
Finally: The *Cornea* book discusses several conditions that mimic DES in their presentation:

--Conjunctivochalasis
--Superior limbic keratoconjunctivitis (SLK)
--**Floppy eyelid syndrome**

**Floppy eyelid syndrome** (FES) is a condition characterized by upper-lid laxity along with chronic inflammation of the ocular surface. FES pts complain of FBS and mucous discharge that are worse in the morning. The main risk factor for FES is obesity.
Dry Eye Syndrome

FES. Wow.
If you can’t tell, that’s an upper lid so lax it can be pinched like this
FES. Note the fine papillary rxn (another common finding) on the easily-everted lid
Dry Eye Syndrome

Finally: The *Cornea* book discusses several conditions that mimic DES in their presentation:

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--Superior limbic keratoconjunctivitis (SLK)
--**Floppy eyelid syndrome**

**Floppy eyelid syndrome** (FES) is a condition characterized by upper-lid laxity along with chronic inflammation of the ocular surface. FES pts complain of FBS and mucous discharge that are worse in the morning. The main risk factor for FES is obesity. The presumed pathogenic process in FES is that during sleep, their laxity allows the upper lids to evert in response to face-rubbing against a pillow while sleeping in the prone position. Lid eversion results in contact between the eye and the bedding which traumatizes the ocular epithelia.
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Floppy eyelid syndrome (FES) is a condition characterized by upper-lid laxity along with chronic inflammation of the ocular surface. FES pts complain of FBS and mucous discharge that are worse in the morning. The main risk factor for FES is obesity. The presumed pathogenic process in FES is that during sleep, their laxity allows the upper lids to evert in response to face-rubbing against a pillow while sleeping in the prone position. Lid eversion results in contact between the eye and the bedding which traumatizes the ocular epithelia.

Initial management is conservative—ointment qHS, and preventing eversion by shielding the eye or taping them shut during sleep. If FES fails to respond to this, surgical tightening of the lax upper lid is in order. FES is strongly associated with obstructive sleep apnea, and all FES pts should be evaluated for OSA.
That’s it! Go through this slide-set a couple of times (at least) until you feel like you have a handle on it. When you’re ready, do slide-set K48, which covers this material in a Q&A format (and more detail).